Clinical Policy: Critical Issues in the Management of Adult Patients Requiring Endotracheal Intubation in the Emergency Department

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ABSTRACT

This clinical policy from the American College of Emergency Physicians is a new policy developed to identify the best evidence available to reduce peri-intubation hypoxemia and/or hypotension in emergent intubations. A writing subcommittee conducted a systematic review of the literature to derive evidence-based recommendations to answer the following clinical questions: (1) For adult patients presenting to the emergency department requiring endotracheal intubation, are there periprocedural interventions that can reduce the incidence of peri-intubation hypoxemia?; (2) For adult patients presenting to the emergency department requiring endotracheal intubation, are there peri-procedural interventions can reduce the incidence of peri-intubation hypotension? Evidence was graded and recommendations were made based on the strength of the available data.

INTRODUCTION

Airway management is core to the practice of emergency medicine. Emergency physicians are often required to perform emergent endotracheal intubation. Though usually safely accomplished in the emergency department (ED) using rapid sequence intubation (RSI), or less commonly through delayed sequence intubation or awake intubation, it is nonetheless a high-risk procedure. Approximately 17% of ED intubations are complicated by peri-intubation major adverse events, defined as hypoxemia, hypotension or cardiovascular collapse, and cardiac arrest.[1] As might be predicted, patients intubated for acute respiratory failure or cardiovascular instability are at increased risk of peri-intubation hypoxemia and cardiovascular collapse. The risk of peri-intubation cardiac arrest is highest among the least stable cohort of patients, including those who are so unstable as to preclude preintubation optimization measures.[1-4]

Patients in the ED requiring intubation have a wide variety of clinical conditions that must be taken into consideration, but given the nonelective nature of these intubations, the common thread is that most patients are potentially or overtly unstable. The concept of the "physiologically difficult airway" has gained traction in recent years.[5] It refers to the physiologic derangements in critically ill patients who place those with limited reserves at particular risk of unwanted side effects of induction, intubation, and initiation of positive-pressure ventilation. Successful intubation requires not only appropriate endotracheal tube placement, but also efforts to optimize the patient's physiology to avoid hypoxemia and hypotension. Accordingly, at least one other airway management guideline has shifted focus from the mechanics of intubation to peri-intubation physiology.[6]

This guideline addresses strategies to minimize peri-intubation physiologic decompensation. We reviewed the evidence for periprocedural interventions that reduce the incidence of hypoxemia and hypotension. Another outcome measure worth mentioning is first-pass success (FPS). The need for multiple sequential intubation attempts is associated with hypoxemia, aspiration, esophageal intubation, hypotension, and cardiac arrest.[7] Although FPS has been used as a primary outcome in many ED-based airway studies, it is a surrogate outcome measure and was therefore not used as the outcome of choice for these critical questions. Although the body of this policy seeks to be informative and provide the supportive data and reasoning for the recommendations provided, it is not comprehensive. Additional data can be found in the Evidentiary Table.

A major challenge with synthesizing literature to form recommendations for ED airway management is that the population of emergency patients is heterogeneous. What may be best for the majority of patients may not be ideal for an individual patient due to particularities of their anatomy or physiology. Thus, this policy is intended to identify the medical or procedural approaches that are best for a general population of patients presenting in emergent need of airway management, recognizing that there is not a "one size fits all approach" because of the nuances of each individual case in the ED. Nonetheless, the strategies recommended below are part of the foundation for improved outcomes in airway management by emergency physicians.

METHODOLOGY

This American College of Emergency Physician (ACEP) clinical policy was developed by emergency physicians with input from medical librarians and a patient safety advocate; is based on a systematic review and critical, descriptive analysis of the medical literature; and is reported in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines.[8]

Search and Study Selection

This clinical policy is based on a systematic review with critical analysis of the medical literature meeting the inclusion criteria. Searches of PubMed, Science Direct, Scopus, EMBASE, and the Cochrane Database of Systematic Reviews were performed by a librarian. Search

terms and strategies were peer reviewed by a second librarian. All searches were limited to human studies published in English. Specific keywords/phrases, years used in the searches, dates of searches, and study selection are identified under the critical question. In addition, relevant articles from the bibliographies of included studies and more recent articles identified by committee members and reviewers were included.

Using Covidence (Covidence, Melbourne, Australia), 2 subcommittee members independently reviewed the identified abstracts to assess for possible inclusion. Of those identified for potential inclusion, each full-length text was reviewed for eligibility. Those identified as eligible were subsequently forwarded to the committee's methodology group (emergency physicians with specific research methodological expertise) for methodological grading using a Class of Evidence framework (Appendix E1, available at http://www.annemergmed.com).

Assessment of Risk of Bias and Determination of Classes of Evidence

Each study identified as eligible by the subcommittee was independently graded by 2 methodologists.

Design 1 represents the strongest possible study design to answer the critical question, which relates to whether the focus was therapeutic, diagnostic, or prognostic, or a meta-analysis. Subsequent design types (eg, Design 2 and Design 3) represent respectively weaker study designs. Articles are then graded on dimensions related to the study's methodological features and execution, including but not limited to randomization processes, blinding, allocation concealment, methods of data collection, outcome measures and their assessment, selection and misclassification biases, sample size, generalizability, data management, analyses, congruence of results and conclusions, and potential for conflicts of interest.

Using a predetermined process that combines the study's design, methodological quality, and applicability to the critical question, 2 methodologists independently assigned a preliminary Class of Evidence grade for each article. Articles with concordant grades from both methodologists received that grade as their final grade. Any discordance in the preliminary grades was adjudicated through discussion which involved at least 1 additional methodologist, resulting in a final Class of Evidence assignment as Class I, Class II, Class III, or Class X (Appendix E2, available at http://www.annemergmed.com). Studies identified with significant methodologic limitations and/or ultimately determined to not be applicable to the critical question received a Class of Evidence grade "X" and were not used in formulating recommendations for this policy. However, content in these articles may have been used to formulate the background and to inform expert consensus in the absence of evidence. Classes of Evidence grading may be found in the Evidentiary Table included at the end of this policy.

Translation of Classes of Evidence to Recommendation Levels

Based on the strength of evidence for the critical question, the subcommittee drafted the recommendations and supporting text synthesizing the evidence using the following guidelines:

Level A recommendations. Generally accepted principles for patient care that reflect a high degree of scientific certainty (eg, based on evidence from one or more Class of Evidence I or multiple Class of Evidence II studies that demonstrate consistent effects or estimates).

Level B recommendations. Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate scientific certainty (eg, based on evidence from one or more Class of Evidence II studies or multiple Class of Evidence III studies that demonstrate consistent effects or estimates).

Level C recommendations. Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of adequate published literature, based on expert consensus. In instances where consensus recommendations are made, "consensus" is placed in parentheses at the end of the recommendation.

There are certain circumstances in which the recommendations stemming from a body of evidence should not be rated as highly as the individual studies on which they are based. Factors such as consistency of results, uncertainty of effect magnitude, and publication bias, among others, might lead to a downgrading of recommendations. When possible, clinically oriented statistics (eg, likelihood ratios, number needed to treat) are presented to help the reader better understand how the results may be applied to the individual patient. This can assist the clinician in applying the recommendations to most patients but allow adjustment when applying to patients with extremes of risk (Appendix E3, available at http://www.annemergmed.com).

Evaluation and Review of Recommendations

Once drafted, the policy was distributed for internal review by members of the entire committee followed by external expert review and an open comment period for all ACEP membership. Comments were received during a 30-day open comment period with notices of the comment

period sent electronically to ACEP members, published in *EM Today*, posted on the ACEP website, and sent to other pertinent physician organizations. The responses were used to further refine and enhance this clinical policy, although responses do not imply endorsement. Clinical policies are scheduled for revision every 3 years; however, interim reviews are conducted when technology, methodology, or the practice environment changes significantly.

Application of the Policy

This policy is not intended to be a complete manual on the evaluation and management of adult patients with endotracheal intubations, but rather a focused examination of a critical question that has particular relevance to the current practice of emergency medicine. Potential benefits and harms of implementing recommendations are briefly summarized within the critical question.

It is the goal of the Clinical Policies Committee to provide evidence-based recommendations when the scientific literature provides sufficient quality information to inform recommendations for the critical question. In accordance with ACEP Resolution 56(21), ACEP clinical policies do not use race-based calculators in the formulation of recommendations. When the medical literature does not contain adequate empirical data to inform the critical question, the members of the Clinical Policies Committee believe that it is equally important to alert emergency physicians to this fact.

This clinical policy is not intended to represent a legal standard of care for emergency physicians. Recommendations offered in this policy are not intended to represent the only diagnostic or management options available to the emergency physician. ACEP recognizes the importance of the individual physician's judgment and patient preferences. This guideline provides clinical strategies for which medical literature exists to inform the critical question addressed in this policy. ACEP funded this clinical policy.

Scope of Application. This guideline is intended for physicians working in EDs.

Inclusion Criteria. This guideline is intended for adult patients aged 18 years and older presenting to the ED who require endotracheal intubation.

Exclusion Criteria. This guideline is not intended for pediatric patients or patients undergoing emergent fiberoptic intubation.

CRITICAL QUESTIONS

(1) For adult patients presenting to the ED requiring endotracheal intubation, are there periprocedural interventions that can reduce the incidence of peri-intubation hypoxemia?

Patient Management Recommandations

Level A recommendations.

Level B recommendations.

When feasible, optimize preoxygenation using noninvasive ventilation (NIV)* over conventional oxygen therapy (COT) for patients being intubated in the ED.

Level C recommendations.

When NIV is not feasible, consider using high-flow nasal cannula (HFNC) for preoxygenation of *hypoxemic patients* being intubated in the ED.

Consider video laryngoscopy (VL) when available for patients being intubated in the ED.

Consider using apneic oxygenation (AO) for patients being intubated in the ED. *(Consensus)*

Potential Benefit of Implementing the Recommendations: Fewer episodes of hypoxemia during and immediately after intubation, reduction of mortality.

Potential Harm of Implementing the Recommendations: Potential for adverse events associated with use of NIV during preoxygenation; potential increase cost related to use of HFNC and NIV, including aspiration.

Keywords/Phrases for Literature Searches:

Intratracheal intubation, airway management, intubation, hypoxia, hypoxemia, rapid sequence intubation, laryngeal masks, emergency department, emergency hospital services, emergency rooms, oxygen deficiency, anoxia.

Study Selection:

A total of 4,845 articles were identified in the searches. Of these, 191 articles were selected from the search results as potentially addressing this question and were candidates for further review. After grading for methodological rigor, 0 Class I studies, 3 Class II studies, and 24 Class III studies were included for this critical question.

Introduction

Peri-intubation hypoxemia and hypoxia are known causes of increased morbidity and mortality.[9] Predictors of oxygen desaturation include preintubation saturation ≤93% (odds ratio [OR] 5.1, 95% confidence interval [CI] 2.3 to 11.0), intubation time >3 minutes (OR 2.7, 95% CI 1.2 to 6.1), and >1 attempt (OR 3.4, 95% CI 1.4 to 8.2).[10] The causes of hypoxemia in the ED population are heterogeneous, and each clinical situation is unique, but there are multiple evidence-based approaches that can be applied to minimize desaturation and reduce the risk of

*Relative contraindications to the use of NIV include patients with increased aspiration risk due to symptoms such as vomiting or decrease level of consciousness and noncompliance due to increased agitation.

adverse events. The included studies tested the use of a procedural checklist, patient positioning, preoxygenation with HFNC, NIV, and bag-valve mask (BVM) during induction, AO, VL versus direct laryngoscopy (DL), bougie, stylet, and the choice of induction medications. Although fiberoptic intubation is a viable option in selected ED patients, we did not review the topic as it is outside the scope of this policy.

Preprocedural preparation: checklists and positioning

In a Class III randomized controlled trial (RCT) of implementing a preintubation checklist for housestaff performing intubations on ICU patients, there was no difference in lowest SpO_2 between the checklist and control groups (92% versus 93%, P=.34).[11] There was no difference across secondary outcomes including the number of laryngoscopy attempts, time to intubation, improved glottic view, severe complications, ventilator free days, ICU free days, or inhospital mortality.[11] Potential significant limitations of this study include the fact that providers may have recalled previous checklist experience, and failure to address the preoxygenation strategy.

A Class III RCT compared ramped positioning (head of the bed elevated to 25°) with the sniffing position (torso supine, neck flexed, and head extended) among 4 ICUs.[12] There was no difference between the median lowest arterial oxygen saturations: 93% (interquartile range [IQR] 84% to 99%) with the ramped position versus 92% (IQR 79% to 98%) with the sniffing position (P=.3). The ramped position did result in more operator-reported difficult intubations (12% versus 5%, P=.04), and fewer successful first-pass intubations (76% versus 85%, P=.02). The primary method of intubation in these patients was DL so these conclusions cannot necessarily be applied to VL intubations.

Preoxygenation and AO

Preoxygenation increases the percentage of oxygen in the lungs during intubation and delays desaturation in the critically ill patient. Multiple techniques have been suggested to optimize preoxygenation beyond COT through facemask (FM) or BVM in the critically ill patient: flush rate oxygen delivery, HFNC, NIV, high fraction inspired oxygen by face mask (HFFM), and active use of a BVM during the apneic period of RSI prior to laryngoscopy.[13-15] One Class II and 6 Class III studies were identified that met inclusion criteria. Numerous studies were excluded because the rate of hypoxemia was not reported.

Gibbs et al[14] performed a Class II RCT in 24 EDs and ICUs which provides supportive evidence for use of NIV prior to intubation. Critically ill patients were randomized to NIV from the beginning of preoxygenation through laryngoscopy or to oxygen mask (FM or BVM). The authors defined hypoxemia as an SpO_2<85% between induction and 2 minutes after intubation. Among the 1,301 patients enrolled, hypoxemia was found in 57 of 624 patients (9.1%) in the NIV group and in 118 of 637 patients (18.5%) in the oxygen-mask group (difference −9.4 percentage points, 95% CI −13.2 to −5.6). Important to note is that cardiac arrest occurred in 1 patient (0.2%) in the NIV group and in 7 patients (1.1%) in the oxygen-mask group (difference −0.9 percentage points, 95% CI −1.8 to −0.1). This study included both ED and ICU patients. It is important to note that patients who required immediate intubation were not included in the study.[14]

Three Class III studies evaluating the effectiveness of NIV had variable results. The first Class III study, a network meta-analysis of 7 RCTs of adult patients with acute hypoxemic respiratory failure, provided support for NIV with or without HFNC over other approaches.[15] Preoxygenation techniques included COT with FM or BVM, HFNC or NIV. Preoxygenation with NIV resulted in less desaturation than HFNC (mean oxygen saturation difference 3.6%, 95% CI 0.6% to 6.6%) and COT (mean oxygen saturation difference 5.5%, 95% CI 2.7% to 8.3%). There was no difference between NIV versus NIV plus HFNC. NIV reduced severe desaturations (SpO_2<80%) compared with COT (OR 0.42, 95% CI 0.19 to 0.97). The second Class III NIV study, an RCT in ICU patients, compared preoxygenation with NIV versus COT with BVM also provided support for the superiority of NIV.[16] Following preoxygenation, the median SpO_2 was higher in the NIV group (98% versus 93%, P=.001). During the intubation, lower median SpO_2 values were observed in the BVM group (81% versus 93%, P=.001) compared with the NIV group. Twelve (46%) patients in the BVM group and 2 (7%) in the NIV group had an SpO_2 <80% (P=.01).

In contrast, a Class III study compared NIV with HFNC in 28 ICU patients with acute hypoxemic respiratory failure found no difference in the frequency of severe hypoxemia (SpO_2<80%) (absolute difference –4.2%, 95% CI –13.7 to 5.5) or late complications.[17]

Two Class III studies that compared HFNC alone (without NIV) with COT had conflicting results. The first, which showed a benefit with HFNC, was an RCT comparing preoxygenation with HFNC versus BVM among nonseverely hypoxemic ICU patients.[18] Compared with BVM, HFNC patients had a lower relative risk of experiencing an SpO_2<95% (respiratory rate [RR] 0.51, 95% CI 0.26 to 0.99). No significant difference was seen

with severe hypoxemia (SpO_2<80%), which occurred in 2% of HFNC patients and 8% of BVM patients (*P*=.06). The second Class III RCT showed no statistical difference when comparing preoxygenation using HFNC versus HFFM.[19] The lowest median recorded SpO_2 during intubation for the HFNC group was 92% (IQR 80% to 96%) compared with 90% for the HFFM group (IQR 81% to 95%, *P*=.44).[19]

Another Class III study of ICU patients compared BVM ventilation with no ventilation during the interval between induction and laryngoscopy.[20] In the BVM group, 11% experienced an SpO_2<80% versus 23% in the nonventilated group (RR 0.5%, 95% CI 0.3 to 0.8). Similarly, the BVM group also had a lower incidence of SpO_2<90% (30% in the BVM group versus 40% in the nonventilated group [RR 0.8, 95% CI 0.6 to 0.97]). Adverse event rates were similar.

AO is a technique for providing oxygenation during the period of apnea following administration of an anesthetic or paralytic medication. Our search identified 1 Class II and 3 Class III studies of AO and the incidence peri-intubation hypoxia or hypoxemia. A significant challenge in comparing results across studies is differing AO flow rates (low flow=15 L/min versus high flow=50 to 60 L/min) and duration of preoxygenation.

Among the 4 studies meeting inclusion criteria, results were mixed. The first, a Class II RCT, compared AO with >15 LPM of oxygen by nasal cannula versus no AO among ED patients requiring endotracheal intubation.[21] There was no difference in lowest mean SpO_2 (92%, 95% CI 91 to 93 in AO versus 93%, 95% CI 92 to 94 in COT). The second study, a Class III randomized ICU trial, also found no advantage to low flow AO during intubation versus no AO.[22] An SpO_2 of <80% occurred in 16% of the AO patients and 25% of the control group (*P*=.22). SpO_2 of <90% occurred in 45% of patients in the AO group versus 47% of patients in the control group (*P*=.9). A Class III meta-analysis of 6 prospective studies, including 4 RCTs, provided mixed results.[23] Among participants who received AO, SpO_2 of <80% occurred in 15%, versus 21% among those who did not (RR 0.7, 95% CI 0.5 to 1.0). In an analysis of only the 4 RCTs, there was an increase in the AO of lowest SpO_2 value by 3% (95% CI 2.3 to 3.4). Only one of these studies used low flow AO versus all other studies which used high-flow oxygen. In the final study, a Class III study of prospectively collected registry data, the incidence of desaturation was compared between those who received up to 15 L/min of oxygen through nasal cannula during AO with those who did not.[24] Among the patients who received AO, 10% desaturated to <93% versus 14% of those who did not (OR 0.7, 95% CI 0.53 to 0.95).

VL Versus DL

Widespread availability VL in US EDs has altered the standard approach of many emergency physicians to RSI. All of the randomized studies comparing VL with DL report the outcome of FPS, an outcome that is not patient oriented but is associated with hypoxemia. In the summaries below, we report FPS rates in addition to hypoxia outcomes. A complicating factor with the following studies is that these devices come in varying geometries. Video blades may be closer to standard geometry blades or hyperangulated, thus requiring the user to be educated in the different approaches associated with each type of video blade.

Three Class III meta-analyses were included. In the first, Araújo et al[25] compared the use of VL versus DL across 14 studies encompassing 3,981 critically ill patients. There was no difference between VL and DL in the frequency of severe hypoxemia. VL did increase FPS, compared with DL (RR 1.1, 95% CI 1.0 to 1.2, *P*<.01).[25] In the second, De Jong et al[26] identified 6 studies and found a pooled OR for severe hypoxemia of 1.2 (95% CI 0.7 to 2.2, *P*=.46), with substantial heterogeneity among the studies (I2=56%). FPS was more likely among patients intubated using VL (OR 2.0, 95% CI 1.4 to 3.2, I2=68%).[26] In the third meta-analysis, Lewis et al[27] used data from 8 randomized trials. There were no statistically significant differences between the groups with regard to hypoxia (OR 0.4, 95% CI 0.1 to 1.4). FPS was not different between the groups (OR 1.3, 95% CI 0.8 to 2.1, I2=79%).[27]

Only 3 randomized studies of VL versus DL met methodological standards for inclusion in this review. In a Class III RCT, Prekker et al[28] identified no difference in severe hypoxemia. FPS was achieved in 85.1% in the VL group versus 70.8% in the DL group (*P*<.001).[28] In a second Class III RCT, Abdelgalel[29] compared Macintosh laryngoscopy with 2 types of video laryngoscopes in an ICU—Airtraq and Glidescope. Oxygen desaturation <90% occurred in 25% of patients randomized to Macintosh versus 5% in the Glidescope group and 7.5% in the Airtraq group (*P*=.013). FPS occurred in 95% of patients in the Glidescope group, 92.5% of patients in the Airtraq group, and 72.5% patients in the Macintosh group (*P*<.05).[29] In a third Class III RCT, no benefit with VL was identified with hypoxemia occurring in 8% of VL patients and 11% of DL patients (*P*=.37).[30] Severe hypoxemia occurred in 3.4% of VL patients and 0.5% DL patients (*P*=.06). Successful first-pass intubation occurred in 68% of patients in the VL group and 70% in the DL group (*P*=.60).[30]

Bougie and Stylet

Gum elastic bougie devices may facilitate endotracheal intubation. A Class III RCT randomized patients to intubation with a bougie or with just an endotracheal tube and stylet.[31] Hypoxemia occurred in 47 of 371 participants (13%) randomized to bougie versus 50 of 364 participants (14%) randomized to endotracheal tube and stylet (95% CI for absolute risk reduction of 1%, –4% to 6%). Among study participants with a difficult airway characteristic randomized to intubation with a bougie, FPS without hypoxemia occurred in 156 of 191 participants (82%) versus 123 of 177 participants (60%) randomized to endotracheal tube and stylet (95% CI for absolute risk reduction of 12%: 3% to 21%). In a follow-up Class III RCT hypoxemia <80% occurred in 58 (11.0%) of patients in the bougie group and 46 (8.8%) of patients randomized to just endotracheal tube and stylet (absolute risk difference, 2.2 percentage points [95% CI −1.6 to 6.0]).[32] Successful intubation on the first attempt occurred in 80% of the bougie group and 83% of the stylet group for a risk difference of −2.6 percentage points (95% CI −7.3 to 2.2).

In a Class III RCT, Jaber et al[33] randomized patients to intubation with an endotracheal tube plus stylet or endotracheal tube alone. Severe hypoxemia occurred in 69 of 501 patients (13.8%) randomized to endotracheal tube plus stylet and 76 of 498 patients (15.3%) randomized to endotracheal tube alone (P=1.00). FPS occurred in 392 of 501 patients (78.2%) randomized to stylet and 356 of 498 patients (71.5%) randomized to no stylet (P=.01).

Medications

Medication choice may affect peri-intubation physiology. Only 2 methodologically rigorous studies were included—one used fentanyl as an adjuvant to RSI and one compared succinylcholine versus rocuronium. In a Class II study, 302 ED patients were randomized to treatment with or without fentanyl (0.5 to 2 μg/kg) as part of an RSI protocol that also included ketamine and rocuronium.[34] Oxygen saturation <93% within 10 minutes of induction occurred in 28 (19%) of patients in the fentanyl arm and 19 (13%) of patients in the placebo arm (95% CI for absolute risk reduction of 6%: –2% to 15%). In a Class III study, 1,248 patients were randomized to 1 mg/kg succinylcholine or 1.2 mg/kg rocuronium.[35] Intubations were performed by emergency physicians or anesthesiologists. Oxygen saturation <90% occurred in 55 of 610 (9.0%) rocuronium patients and 61 of 616 (9.9%) succinylcholine patients (absolute risk reduction 0.9%, 95% CI –2.6% to 4.4%).

Brief Summary

This policy discusses multiple periprocedural interventions to reduce hypoxemia in adult patients undergoing emergent endotracheal intubation. When feasible, a strategy of preoxygenation with NIV reduces hypoxemia compared with HFNC and conventional preoxygenation strategies. The data for AO are mixed, with some studies showing limited benefit and others none. AO, however, has minimal or no risk and can be provided by HFNC or nasal cannula throughout induction and laryngoscopy. In hypoxemic patients at low risk of aspiration, physicians may also consider utilizing positive-pressure ventilation with BVM in the time interval between induction and laryngoscopy. There was no difference in hypoxic outcomes between those patients intubated with a bougie rather than a stylet or those intubated with an endotracheal tube and stylet versus no stylet, though endotracheal tube and stylet improve FPS versus endotracheal tube alone. Similarly, utilizing VL rather than DL does not decrease the frequency of hypoxemia, though it does improve FPS. The use of preprocedural checklists, medication choice, and patient positioning did not affect hypoxemia. The ramped position had fewer rates of FPS but the study examining it predominantly utilized DL and it is unclear what the effect would be with VL.

Future Research

Future research should focus on the use of NIV to optimize preoxygenation in the undifferentiated ED population. More robust studies utilizing NIV primarily within the ED versus the ICU setting would be helpful in demonstrating clear safety of this practice across all ED environments. In addition, although FPS has shown to be a good surrogate marker for successful airway management, research utilizing hypoxia and hypoxemia as the primary patient-centered outcomes during intubation would enhance the overall strength of available evidence. Finally, studies comparing induction agents with a primary outcome of hypoxia would be useful.

(2) For adult patients presenting to the ED requiring endotracheal intubation, are there periprocedural interventions that can reduce the incidence of peri-intubation hypotension?

Patient Management Recommendations

Level A recommendations. None.

Level B recommendations.

Use etomidate or ketamine as an induction agent to reduce the risk of peri-intubation hypotension in patients requiring endotracheal intubation in the ED.

Level C recommendations.

Avoid the use of fentanyl, midazolam, or propofol as an induction or coinduction agent in patients requiring endotracheal intubation in the ED who are at increased risk for postintubation hypotension.

Potential Benefit of Implementing the Recommendations: Fewer episodes of hypotension during and immediately after intubation; reduced mortality.

Potential Harm of Implementing the Recommendations: Adverse events related to side effects of the induction agents.

Keywords/Phrases for Literature Searches:

Intratracheal intubation, airway management, intubation, hypotension, rapid sequence intubation, laryngeal masks, emergency department, emergency hospital services, emergency rooms, low blood pressure.

Study Selection:

The search identified 5,062 articles. Of these, 92 articles were selected as potentially addressing this question and were candidates for further review. After grading for methodological rigor, 0 Class I studies, 1 Class II study, and 12 Class III studies were included for this critical question.

This critical question focuses on preventing or mitigating peri-intubation hypotension. There are various mechanisms by which induction and intubation cause hypotension, including through the vascular and cardiac effects of pharmacologic agents administered, decreased venous return as a result of positive-pressure ventilation, and reduced sympathetic drive. The studies included in this section examined 2 strategies for reducing the risk of hypotension: the use and optimal dosing of hemodynamically stable induction agent(s) and preintubation fluid resuscitation. Of note, no studies on peri-intubation vasopressor use met methodological criteria for inclusion.

Choice of Induction Agent

Five Class III studies looking at the hemodynamic effects of etomidate and/or ketamine as induction agents met inclusion criteria. The first was a Class III randomized, parallel-group ED trial comparing the incidence of hypotension (systolic blood pressure [SBP] <90 mmHg) after intubation among patients still in the ED receiving etomidate (0.3 mg/kg) versus ketamine (2 mg/kg).[36] There was no difference in the incidence of hypotension between the groups (28% in the ketamine group versus 26% in the etomidate group) (difference 2%; 95% CI –13% to 17%).[36] The second was a Class III, prospective, observational ED study that concluded etomidate (dosed at 0.3 mg/kg) was a hemodynamically stable induction agent.[37] There was a clinically insignificant elevation in SBP and diastolic blood pressure (DBP) immediately after intubation. Similarly, in the subgroup of 80 patients who were hypotensive, the mean SBP increased from 84 mmHg before intubation to 92 mmHg after intubation ($P<.0001$). A Class III analysis of the National Emergency Airway Registry (NEAR), which analyzed prospectively collected data on 6,806 normotensive ED patients in both community and academic hospitals, found etomidate to be more hemodynamically stable than ketamine.[38] Peri-intubation hypotension (SBP<100 mmHg) occurred in 18% of ketamine encounters versus 12% of etomidate encounters (effect size difference 6%, 95% CI 3% to 9%). It is important to note that in this registry, patients receiving ketamine were more likely to have trauma or sepsis as the indication for intubation. Although the association between ketamine and a higher risk of hypotension was seen even after logistic regression analysis controlling for confounders was performed, the conclusions that can be drawn from this observational study about the relative hemodynamic effect of these 2 induction agents are limited.

One Class III randomized trial found no difference between "ketofol" (0.5 mg/kg of ketamine and propofol each) and half-dose etomidate (0.15 mg/kg) in the 5-minute mean arterial pressure as compared with the baseline: "ketofol" (78±15 mmHg at 5 minutes versus 81±13 mmHg at baseline) or the etomidate group (82±17 mmHg versus 83±18 mmHg at baseline) (treatment difference, −2 mmHg; 95% CI −7 to +3 mmHg; $P=.385$). [39] No differences were seen at 15 minutes either.[39] The final Class III study of induction agents was an analysis of data from 977 unstable patients with a shock index ≥0.9 from the second Japanese Emergency Airway Network (JEAN-2), where the use of ketamine was compared with propofol or midazolam.[40] Ketamine was associated with a lower risk of postintubation hypotension (SBP of ≤90 mmHg or ≥20% decrease in SBP) than the reference group of midazolam or propofol use (15% versus 27%; OR 0.5; 95% CI 0.3 to 0.7).[40]

Dose of Induction Agent

One Class III retrospective analysis of the NEAR data looked at the relationship between the dose of etomidate or ketamine and risk of postintubation hypotension (SBP<100 mmHg).[41] Neither a lower dose of ketamine (1.0 versus 1.3 mg/kg) nor a lower dose of etomidate (0.1 versus 0.3 mg/kg) was associated with a lower risk of hypotension. There was no difference in outcome when patients who were already hypotensive prior to intubation, nor those intubated for shock, were excluded. When the average dose of induction agent was compared between those having postintubation hypotension versus those who remain hemodynamically stable, there was also no

difference. In the aforementioned Class III NEAR analysis, which only included normotensive patients, there was also no association between dose of etomidate ($\leq$0.3 versus >0.3 mg/kg) or ketamine ($\leq$1.0 versus >1.0 mg/ kg) and hypotension.[38] Given the available literature, no firm conclusion on dosing can be drawn at this time.

Pretreatment and Coinduction Agents

This Class II study was a randomized ED trial of fentanyl (200 μg/mL) versus placebo as a coinduction agent with ketamine to ameliorate both postintubation hypertension and hypotension.[34] The average preintubation SBP was normal, with 12% in both groups receiving vasopressors. In this relatively stable study cohort, hypotension was more common in the fentanyl group versus the placebo group (29% versus 16%; difference 13%, 95% CI 3% to 23%). A Class III analysis of hemodynamically stable ED patients in the JEAN 2 study also found fentanyl (administered as a pretreatment agent) to be significantly associated with postintubation hypotension.[42] Induction agents administered were most commonly midazolam, followed by propofol and ketamine. Those who received fentanyl had a higher risk of postintubation hypotension compared with those who did not receive fentanyl (17% versus 6%) (OR 1.73; 95% CI 1.01 to 2.97).

Fluid Bolus Administration

The Class III PrePARE study was an RCT evaluating the potential benefit of a 500 mL crystalloid bolus started prior to induction and infused during the intubation procedure.[43] There was no difference in the primary endpoint of cardiovascular collapse (SBP<65 mmHg) between the fluid bolus group and the no fluid bolus group (20% versus 18%, absolute difference of 1%; 95% CI –7% to 10%). The fact that patients were excluded in cases where the treating physician judged them to need a fluid bolus limits the conclusions that can be drawn for the purposes of this discussion. In addition, almost all patients were in the ICU, and had already received fluid bolus administration prior to being enrolled in the study (the amount was not recorded), which also differs from many ED patients requiring intubation. Finally, the endpoint of cardiovascular collapse (SBP<65 mmHg) was also more stringent than the outcome measure of any degree of peri-intubation hypotension. The Class III PrePARE II RCT also examined the hemodynamic effect of a fluid bolus (infused prior to induction, when possible), but included patients receiving positive-pressure ventilation between induction and laryngoscopy.[44] There was no difference in the risk of cardiovascular collapse between the groups (21% and 18% in the fluid bolus and control group, respectively) (95% CI –2% to 8%). This trial had similar limitations as PrePARE I, and therefore no recommendations were made regarding fluid resuscitation in the ED population.

Brief Summary

Peri-intubation hypotension is associated with a higher risk of adverse events in patients undergoing emergent intubation. Methods to optimize patients' physiology to potentially reduce this risk during intubation include fluid bolus administration, induction agent selection, dosing adjustment, and the use of vasopressors, but the overall available literature to drive recommendations is limited at this time. Given the methodological criteria of this review, evidence surrounding the use of ketamine and etomidate reflects their overall safety and efficacy in this generally critically ill patient population. Likewise, limiting the use of fentanyl during intubation when hypotension is a concern should be considered.

Future Research

Our current knowledge finds equipoise between how ketamine and etomidate may affect postintubation hypotension. Future dedicated trials may delineate subgroups of patients who may benefit from one versus another agent. Future research may expand on how peri-intubation vasopressor agents and/or intravenous fluid boluses may or may not reduce the risk of hypotension in the ED population.

Relevant industry relationships: There were no relevant industry relationships disclosed by the subcommittee members for this topic.

Relevant industry relationships are those relationships with companies associated with products or services that significantly influence the specific aspect of disease addressed in the critical question.

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Appendix E1. Literature classification schema.*

Design/Class	Therapy†	Diagnosis‡	Prognosis§
1	Randomized, controlled trial or meta-analysis of randomized trials	Prospective cohort using a criterion standard or meta-analysis of prospective studies	Population prospective cohort or meta-analysis of prospective studies
2	Nonrandomized trial	Retrospective observational	Retrospective cohort Case control
3	Case series	Case series	Case series

*Some designs (eg, surveys) will not fit this schema and should be assessed individually.
†Objective is to measure therapeutic efficacy comparing interventions.
‡Objective is to determine the sensitivity and specificity of diagnostic tests.
§Objective is to predict outcome, including mortality and morbidity.

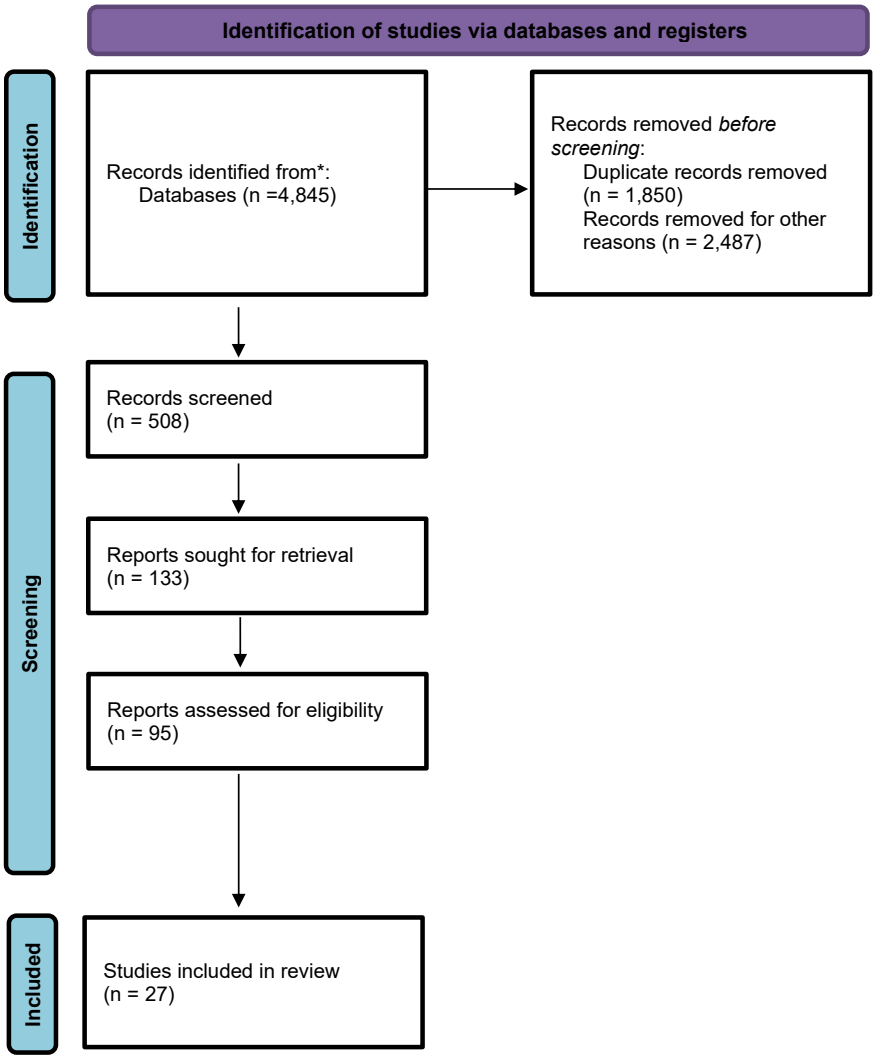
Appendix E2. Approach to downgrading strength of evidence.

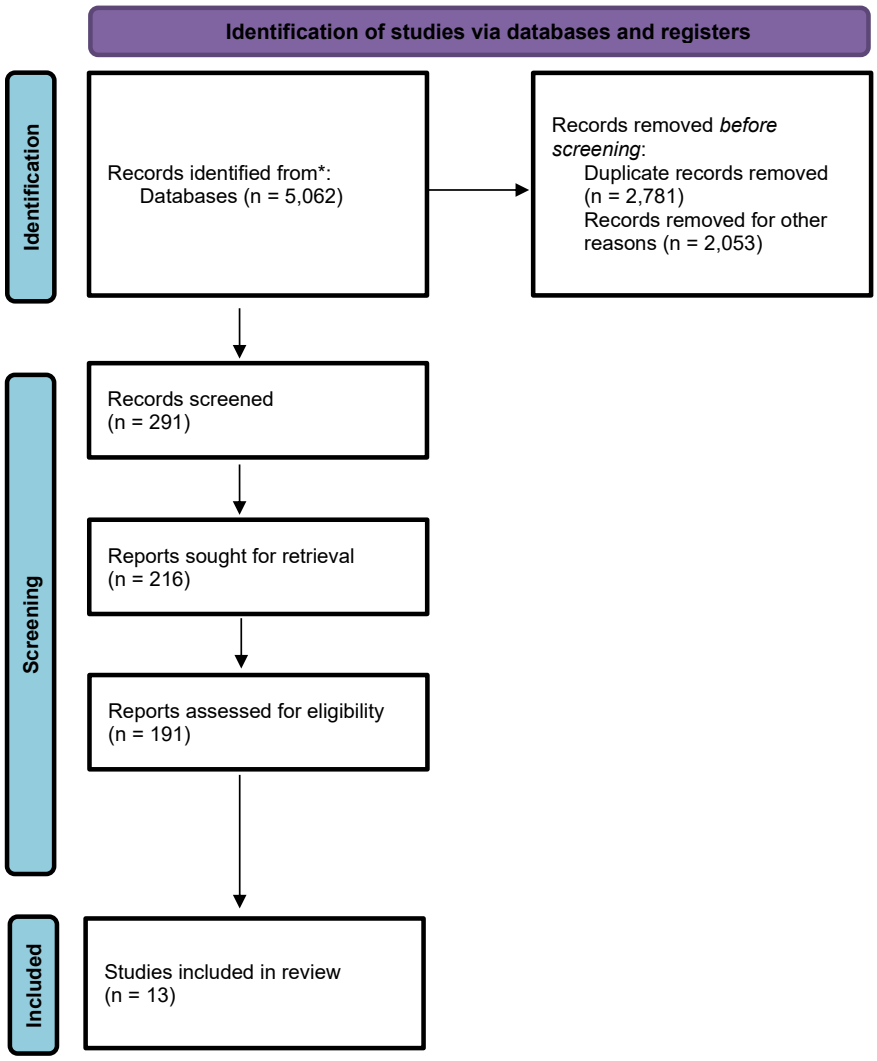
	Design/Class		
Downgrading	**1**	**2**	**3**
None	I	II	III
1 level	II	III	X
2 levels	III	X	X
Fatally flawed	X	X	X

Appendix E3. Likelihood ratios (LRs) and number needed to treat.*

LR (+)	LR (–)	
1.0	1.0	Does not change pretest probability
1–5	0.5–1	Minimally changes pretest probability
10	0.1	May be diagnostic if the result is concordant with pretest probability
20	0.05	Usually diagnostic
100	0.01	Almost always diagnostic even in the setting of low or high pretest probability

*Number needed to treat (NNT): number of patients who need to be treated to achieve 1 additional good outcome; NNT=1/absolute risk reduction×100, where absolute risk reduction is the risk difference between 2 event rates (ie, experimental and control groups).


Identification of studies via databases and registers
Identification
Records identified from*:
Databases (n =4,845)
Records removed *before screening*:
Duplicate records removed (n = 1,850)
Records removed for other reasons (n = 2,487)
Screening
Records screened
(n = 508)
Reports sought for retrieval
(n = 133)
Reports assessed for eligibility
(n = 95)
Included
Studies included in review
(n = 27)


Identification of studies via databases and registers
Identification
Records identified from*:
Databases (n = 5,062)
Records removed *before screening*:
Duplicate records removed (n = 2,781)
Records removed for other reasons (n = 2,053)
Screening
Records screened
(n = 291)
Reports sought for retrieval
(n = 216)
Reports assessed for eligibility
(n = 191)
Included
Studies included in review
(n = 13)

Evidentiary Table.

Author and Year of Publication	Class of Evidence	Setting and Study Design	Methods and Outcome Measures	Results	Limitations and Comments
Abdelgalel (2018)[29]	III for Q1	RCT in an Egyptian surgical intensive care unit (SICU) testing DL versus VL	Included adult SICU patients ASA III or IV who required emergent intubation; participants randomized to Macintosh direct, Glidescope VL, or Airtraq VL; critical care physicians with ≥30 intubations with each video device; primary outcome was FPS; secondary outcomes included hypoxia defined saturation <90%	Oxygen desaturation occurred in 10/40 (25%) in Macintosh group, 2/40 (5%) in Glidescope, and 3/40 (7.5%) in Airtraq (*P*=.013) FPS occurred in 29/40 (72.5%) in the Macintosh group, 38/40 (95%) in the Glidescope group, and 37/40 (92.5%) of the Airtraq group (*P*=.005)	Indirect evidence patients were intubated in the SICU; single center in Egypt might not be generalizable; intubations done only by experienced physicians not trainees; methods for preoxygenation and preintubation saturation not reported
Araújo et al (2024)[25]	III for Q1	Systematic review and meta-analysis of VL versus DL in the ED or ICU	Included studies were RCTs conducted among adults in an ICU or ED. The primary outcome for the study was FPS. Severe hypoxemia defined as oxygen saturation <80% was reported as a safety endpoint	14 studies with 3,981 patients were included Rates of severe hypoxemia were comparable (RR 0.98, 95% CI 0.74-1.29, *P*=.87, I^2=22%) Compared with DL, VL increased the rate of FPS (RR 1.12, 95% CI 1.04-1.20, *P*<.01, I^2 =82%) Neither location of intubation (*P*=.48) nor operator experience (*P*=.42) impacted outcomes	13 studies carried high risk of bias due to unblinding of outcome adjudicators; 7 studies had potential bias due to the inexistence of protocols; funnel plot and Egger's test (*P*=.048) suggested publication bias; heterogeneity was evident in primary outcome but not for severe hypoxemia

Baillard et al (2006)[16]	III for Q1	RCT in 2 French ICUs testing preoxygenation with noninvasive ventilation (NIV) versus nonrebreather BVM (NRBM)	Included patients with hypoxemic respiratory failure who required intubation Outcome measures: lowest mean saturation during intubation, patients with O_2 saturation <80% during intubation, patients with O_2 saturation <92% during preoxygenation	57 patients were randomized; outcome data available for 26 control and 27 NIV patients Lowest mean saturation during intubation: 93% in NIV versus 81% in NRBM group $P<.001$ Patients with saturation <80% during intubation: 2/27 NIV versus 12/26 NRBM ($P<.01$) Patients with saturation <92% during preoxygenation: 1/27 NIV versus 8/26 NRBM ($P=.02$)	Study is indirect evidence because ICU location with intubations done by experienced critical care physicians; physicians were not blinded to the use of NIV; those extracting outcomes were not blinded to the intervention; one patient in the NIV group was excluded because of inability to use it; it is unclear whether some patients in the control arm might have also failed NIV use
Binks et al (2017)[23]	III for Q1	Meta-analysis of AO with high flow in ICU	Outcomes: lowest SpO_2, frequency of critical hypoxia	4 studies, 353 patients for lowest SpO_2 during intubation: mean benefit of 2.8% (95% CI 2.3-3.4) favoring ApOx with high flow; $I^2=0$ 6 studies, 508 patients for saturation <80% during intubation (RR 0.69, 95% CI 0.48-1.0) favoring ApOx with high flow; $I^2=21\%$	Meta-analysis is indirect evidence because only studies located in the ICU were included; studies included prospective cohort and RCTs; the fixed effects model was used; no heterogeneity for the desaturation outcomes; 2 studies were low quality—it is unclear if low-quality studies were used for the desaturation outcomes

					and if so, there was no sensitivity analysis done after removing low-quality studies
Bodily et al (2016)[10]	III for Q1	Retrospective cohort study of all RSIs in a single academic ED	Determined frequency and predictors of saturation <90% using data captured as part of clinical care	166 patients with available data. Desaturation occurred in 59/166 (36%). Predictors of desaturation <90% include preintubation SpO_2<93%, intubation time >3 minutes, >1 attempt	During the study period, use of apneic (passive) nasal oxygenation during the RSI attempt was not common; intubations were with DL only; no power calculation was reported; data analyzed with logistic regression with limited numbers of patients and therefore potential confounder variables were excluded; cases with missing data dropped – 14% no documentation of intubation method
Caputo et al (2017)[21]	II for Q1	Unblinded RCT of AO with flush rate oxygen by nasal cannula	Included adults requiring RSI who received at least 3 minutes of adequate preoxygenation. Randomized to AO with >15 LPM oxygen by nasal cannula or no AO. Blinded outcome assessors. The primary outcome was average lowest oxygen recorded during the apneic period or 2 minutes after.	206 patients were enrolled. Primary pulmonary etiologies were the most common reasons for intubation. Mean lowest SpO_2 was 92% in the AO group and 93% in the usual care group (P=.08). 17% of the AO group experienced saturation <90% versus 15% of usual care. 3% of the AO group experienced	Unblinded; outcomes self-reported by providers who may have underestimated adverse events and time to intubation; single-center study might not generalize; desaturation outcomes not primary; induction agents were not

			Also reported desaturation <90% and <80%	saturation <80% versus 4% of usual care	reported by arm
Casey et al (2019)[20]	II for Q1	Multicenter RCT in ICU comparing BVM versus no ventilation after induction	Compared BVM versus no ventilation during period between induction and laryngoscopy among ICU patients intubated for any reason Outcomes: mean lowest oxygen saturation and frequency of saturation <80%	401 patients were enrolled. 97.5% received neuromuscular blockade Mean lowest saturation was 96% in BVM and 93% in no ventilation (*P*=.01) 11% in the BVM group versus 23% in the no ventilation group had saturation <80% A new opacity on chest x-ray during the 48 hours after intubation was reported in 16.4% of ventilated patients and 14.8% of nonventilated patients (*P*=.73)	Indirect evidence patients were treated only in ICUs; NIV was not allowed if in the study; AO was allowed but not standard in study arms; unblinded study with data collection recorded in real time by a research team member familiar with the study outcome; no ventilation group had 11% more patients with pneumonia; ~30% higher rates of BVM for preoxygenation in the BVM group; post hoc adjustments were done to account for imbalances; unclear relevance to ED patients who may have eaten more recently
De Jong et al (2014)[26]	III for Q1	Systematic review and meta-analysis of VL versus DL for ICU patients. ED patients were excluded from this analysis	Included studies of ICU patients that compared VL to DL	6 studies involving 1,186 patients had data on severe hypoxemia. Odds of severe hypoxemia were greater in VL (OR 1.24, 95% CI 0.70-2.19) though there was substantial heterogeneity	Indirect evidence only studies with ICU patients were included and specifically excluded patients in the ED; included RCTs, prospective and

				(I^2=56%) The pooled OR for FPS was 2.07 (95% CI 1.35-3.16, *P*<.001) for VL versus DL	retrospective cohort studies; hypoxemia was a secondary outcome; there was significant heterogeneity for the hypoxemia outcome; sensitivity analysis was done to adjust for heterogeneity
Driver et al (2018)[31]	II for Q1	ED-based RCT of bougie versus endotracheal tube and stylet	Pragmatic RCT of bougie versus endotracheal tube plus stylet in a center with extensive experience using bougie as initial approach to intubation Trained, unblinded research associates collected outcome data Hypoxemia was defined as an oxyhemoglobin saturation <90% (or, if the attempt began with a saturation <90%, an absolute decrease in saturation of >10%) The trial's primary outcome was FPS among patients with at least one difficult airway feature Duration of procedure was recorded from time laryngoscope entered the	757 patients were randomized of whom 380 had a difficult airway characteristics Hypoxemia occurred in 47/371 (13%) of participants randomized to bougie versus 50/364 endotracheal tube + stylet participants (14%) (95% CI for absolute risk reduction of 1%, –4% to 6%, *P*=.67) Among study participants with a difficult airway characteristic randomized to intubation with a bougie, first-attempt success without hypoxemia occurred in 156/191 (82%) versus 123/177 (60%) randomized to endotracheal tube and stylet (95% CI for absolute risk reduction of 12%: 3%-21%, *P*=.006)	The study was conducted in a single institution with extensive experience in bougie use; unblinded outcome assessment; 7% of patients randomized to the endotracheal tube + stylet group were intubated using a bougie on the first attempt (protocol violation); this was ascribed to anticipated difficulty or need for rapid intubation; assumption of proportional hazards between groups for first-attempt duration was not upheld; hypoxemia was secondary outcome; bougie group had more patients with

			mouth until it was removed	Duration of procedure 38 seconds bougie versus 34 seconds for endotracheal tube and stylet; absolute difference, 4 seconds (95% CI 2-7)	saturations <80% prior to intubation
Driver et al (2021)[32]	III for Q1	Multicenter RCT of bougie versus endotracheal tube and stylet	A multicenter replication study of Driver 2018 Unblinded, pragmatic RCT of bougie versus endotracheal tube and stylet conducted in 15 EDs and ICUs A trained data collector assessed outcomes Hypoxia: saturation <80% during the interval between induction and 2 minutes after tracheal intubation	1,106 patients were randomized Hypoxemia <80% occurred in 58 (11.0%) of patients in the bougie group and 46 (8.8%) of patients randomized to endotracheal tube and stylet Successful intubation on the first attempt occurred in 447 patients (80.4%) in the bougie group and in 453 patients (83.0%) in the stylet group, for a risk difference of −2.6 percentage points (95% CI −7.3 to 2.2; *P*=.27) Median duration of the intubation was 124 seconds (97-180) in the bougie group and 112 (85-157) in the stylet group for a median difference of 12 seconds (95% CI 4-20 seconds)	Indirect evidence because ED and ICU patients recruited; it was a randomized trial, pragmatic, not concealed allocation; bougie versus endotracheal tube with stylet; controlled for VL versus DL; oxygen saturation < 80% was planned secondary outcome; multiple other preoxygenation maneuvers could have been done; also excluded critical patients who were decompensating

Ferguson et al (2022)[34]	II for Q1	Multicenter, randomized, blinded, placebo-controlled trial of patients undergoing RSI in 5 Australian EDs	Patients were induced with either fentanyl (200 µg) versus placebo plus standard induction with ketamine (average dose of 1.3 mg/kg) and rocuronium 1.5 mg/kg Primary outcome was postintubation SBP outside the range of 100-150 mmHg (or if they were hypotensive at induction, a drop in SBP >10%) within the first 10 minutes Secondary outcomes included hypoxia (SpO_2≤93%), tachycardia (HR≥120), and cardiac arrest occurring within 10 minutes of induction	302 patients were randomized; 290 analyzed, but 13 of 290 did not have follow-up data; 277 in final analysis Hypoxia occurred in 28/140 (19%) of fentanyl group versus 19/137 (13%) of placebo group. 95% CI for difference of 6% –2% to 15% FPS occurred in 132 (92%) of fentanyl patients and 92% (136) of placebo patients. 95%CI for difference of 0: –6% to 6%)	Direct evidence from 5 EDs in Australia; hypoxia was planned secondary outcome; likely underpowered for reported difference of 6%; patients were not recruited overnight due to staffing limitations; missing data addressed with sensitivity analysis assuming all have extreme outcomes; CONSORT diagram did not include loss to follow-up
Frat et al (2019)[17]	III for Q1	Multicenter trial across 28 French ICUs comparing NIV and HFNC for risk of severe hypoxemia during intubation	Patients undergoing intubation for acute hypoxemic respiratory failure (PaO_2:FiO_2 ratio ≤300 mmHg), were randomly assigned to preoxygenation with NIV or HFNC. Severe hypoxemia (pulse oximetry<80%) during procedure served as the	313 patients were included in the intention-to-treat (ITT) analysis. Severe hypoxemia occurred in 33 of 142 (23%) patients after preoxygenation in NIV group and 47 of 171 (27%) in HFNC group (difference –4·2%, 95% CI –13.7 to 5.5) Severe hypoxia risk was	Indirect evidence study in ICUs; unblinded study but data analysts were blinded; informed consent required to participate prior to intubation led to selection of less urgent intubations; less than half of patients meeting inclusion criteria enrolled; many

			primary outcome	not changed with use of either NIV or HFNC. There was a trend for improved hypoxia in patients with moderate to severe hypoxemia with NIV	more patients were randomized to the HFNC group 175 versus 147, implying failures in block randomization; analysis did not adjust for clustering by institution or operators
Fong et al (2019)[15]	III for Q1	Network meta-analysis of preoxygenation with COT versus HFNC versus NIV	Meta-analysis of preoxygenation strategies among patients with acute hypoxemic respiratory failure between induction of anesthesia and initiation of laryngoscopy The primary outcome was the lowest oxygen saturation during intubation Hypoxia outcome was the proportion of patients with saturation <80%	Seven studies were included in the meta-analysis; 3 were at low risk of bias Patients preoxygenated with NIV had significantly less desaturation than patients treated with COT (network estimate, mean oxygen saturation difference [MD] 5.53, 95% CI 2.71-8.34) and HFNC (network estimate, MD 3.58, 95% CI 0.59-6.57) SpO_2<80% was less common in patients preoxygenated with NIV than that with COT (network estimate OR 0.43, 95% CI 0.19-0.97) Analyses of the combination of HFNC +	Indirect evidence, studies were conducted in ICUs; limited number of studies included; some studies of moderate to low quality, but sensitivity analyses were performed and low heterogeneity

				NIV were underpowered	
Gibbs et al (2024)[14]	II for Q1	Multicenter unblinded randomized, unblinded, parallel-group trial comparing preoxygenation with NIV or an oxygen mask conducted at 24 US sites (7 EDs and 17 ICUs) in 15 medical centers. Critically ill adults (age ≥18 y) undergoing tracheal intubation were eligible. Exclusions include pregnancy, a prisoner, or patients already receiving positive-pressure ventilation, had apnea or hypopnea, or had an immediate need for tracheal intubation that precluded randomization or if operator felt NIV contraindicated	The primary outcome was hypoxemia during intubation, defined as oxygen saturation of <85% during the interval between induction and 2 minutes after tracheal intubation. The secondary outcome was the lowest oxygen saturation during the interval between induction and 2 minutes after tracheal intubation. Exploratory outcomes included hemodynamic events potentially from positive-pressure ventilation or from severe hypoxemia, including hypotension (systolic blood pressure, <65 mmHg), new or increased use of vasopressors, and cardiac arrest during the interval between induction and 2 minutes after tracheal intubation Safety outcomes included aspiration during intubation, as reported by the operator; a new infiltrate identified on chest imaging in the 24 hours after induction; and	Hypoxemia during the interval between induction and 2 minutes after intubation (the primary outcome) occurred in 57/624 patients (9.1%) in the NIV group and in 118/637 patients (18.5%) in the oxygen-mask group (absolute risk difference, −9.4 percentage points; 95% CI −13.2 to −5.6; *P*<.001) During the interval between induction and 2 minutes after tracheal intubation, an oxygen saturation of <80% was found in 39/624 patients (6.2%) in the NIV group and in 84/637 patients (13.2%) in the oxygen-mask group (absolute risk difference, −6.9 percentage points; 95% CI −10.2 to −3.7). Cardiac arrest during the interval between induction and 2 minutes after tracheal intubation occurred in 1/645 patients (0.2%) in the NIV group and in 7/656 patients (1.1%) in the oxygen-mask group	Indirect evidence, 73.2% of patients recruited from ICUs versus 26.8% in EDs; results not stratified by location; unblinded study, unblinded analyses; limited number of trauma patients included in the analysis; patients on NIV before preoxygenation or with vomiting excluded from the study

			the oxygen saturation and FiO_2 at 24 hours after induction	(absolute risk difference, −0.9 percentage points; 95% CI −1.8 to −0.1) 73.2% of patients were ICU and 26.8% were ED patients. In total, 85.9% of the intubations were performed by a resident or a fellow	
Guihard et al (2019)[35]	III for Q1	Out-of-hospital RCT of rocuronium versus succinylcholine	Study conducted in the French out-of-hospital system in which emergency physicians or anesthesiologists intubate in the field in mobile ICUs Included patients were those deemed to need endotracheal intubation by the treating physician Succinylcholine dose was 1.0 mg/kg; rocuronium dose was 1.2 mg/kg The hypoxia outcome was saturation <90% The study's primary outcome was successful first-pass intubation	1,248 patients were randomized Oxygen saturation <90% occurred in 55/610 (9.0%) of rocuronium patients and 61/616 (9.9%) of succinylcholine patients (95% CI for absolute risk reduction of 0.9%: –2.6% to 4.4%) Successful first-pass intubation occurred in 455/610 (74.6%) rocuronium patients and 489/616 (79.4%) succinylcholine patients	Indirect evidence intubations occurred on scene by EMS providers; assignment was concealed but physicians performing the procedure were not blinded to medication and were also the outcome assessors
Guitton et al (2019)[18]	III for Q1	Multicentered, randomized, controlled, open-label trial in 7 French ICUs (4 medical, 2 Med-Surg, 1 surg), prospective cohort. Inclusion: ICU adult patients w/o	Intervention: BVM w/ self-inflatable resuscitator at 15 LPM versus HFNC at 60 LPM. Drugs and NMB left up to physician	192 patients randomized from April 2016 to June 2017. Ultimately 184 included in ITT analysis and 183 in per protocol	Indirect evidence studies conducted in ICUs; patients with severe hypoxemia prior to intubation

		severe hypoxemia (PaO_2/FiO_2 <200). Exclusion: non-ICU patients, fiberoptic intubation, asphyxia, any NP obstruction, known Cormack-Lehane 4 airway, Pts under legal protection, pregnancy, lack of consent, or prior extubation failure. Randomization done in blocks of 6 in a 1:1 ratio Performed both an ITT and per protocol analysis	discretion. HFNC left on for ApOx. Stylet addition first line for difficult airway. Endotracheal tube confirmed by $ETCO_2$ Primary endpoint: median lowest SpO_2 during intubation (beginning of laryngoscopy to mechanical ventilation [MV]) Secondary: SpO_2 from preoxy to MV, intubation difficulty scale, rate of difficult intubation, need for BVM, severe adverse events (death, cardiac arrest, SpO_2<80%, severe hypotension, pressor initiation or >30% increase), moderate (arrythmia requiring intervention, esophageal intubation, vomiting with aspiration, dental injury) SOFA score day 5, length of stay (LOS) in ICU, VAP, and 28-day mortality Planned sample size 192	analysis. Median PaO_2/FiO_2 318 in HFNC and 375 in SMO. Junior operators 84% Primary: ITT analysis no sig difference HFNC 100% (97-100) versus SMO 99% (95-100) *P*=.30. Per Protocol *P*=.26. Lowest SpO_2 during intubation ranged from 69% to 100% and 43% to 100% in HFNC and SMO Median SpO_2 in both groups after PreOx was 100% Secondary: 12% HFNC versus 23% SMO SpO_2 <95% (RR 0.51, 95% CI 0.26-0.99, *P*=.045). 6% versus 14% SpO_2<90% (*P*=.06). 2% versus 8% SpO_2<80% (*P*=.06). 6% versus 19% had one intubation complication (RR 0.31, 95% CI 0.13-0.76, *P*=.007). Severe complications 6% versus 16% (RR 0.38, 95% CI 0.15-0.95, *P*=.03). 0% versus 7% moderate complications	excluded; 8 less patients were randomized to the SMO arm; unblinded study

				P=.01. HFNC associated with less desaturation <90%, less intubation-related complication and a trend to reduce oxygen desaturation <80% (*P*=.058) Similar durations of MV 3 versus 3 (*P*=.80). No difference in SOFA score after 5 days and LOS in ICU (*P*=.89). Mortality rate on day 28 27% (*P*=.93)	
Jaber et al (2021)[33]	III for Q1	Multicenter ICU-based RCT in France	Randomized, unblinded study of endotracheal tube + stylet versus endotracheal tube alone among ICU adult patients requiring intubation; FPS was the primary outcome; severe hypoxemia (<80%) was a secondary outcome; the investigators also report lowest oxygen saturation	999 patients were enrolled; acute respiratory failure was the indication for intubation among 48% of participants; severe hypoxemia occurred in 69/501 (14%) of stylet patients and 76/498 (15%) no stylet patients (95% CI for difference of 1.5%: –4.6% to 7.5%) Lowest mean saturation in the stylet group was 92.8% (SD 7.4%) versus 92.9% (SD 7.9%), *P*=.46 FPS occurred in 392/501 (78%) of stylet patients and 356/498 (72%) of no stylet patients (difference 7%,	Indirect evidence study done in ICUs; hypoxia was secondary outcome; unblinded open RCT but with concealed allocation; user discretion was done for type of blade—mac versus miller, size of endotracheal tube, and other peri-intubation procedures some of which are not reported in the baseline characteristics

				95% CI 1.4%-12%), *P*=.01	
Janz et al (2018)[11]	III for Q1	Prospective, randomized, multicentered trial (3 sites) Inclusion: adult patients intubated by a pulmonary/critical care fellow or anesthesia resident in ICU Exclusion: awake intubation, too emergent, or treating clinician felt a different specific preintubation or patient position was needed 1: 1 randomization	Intervention: checklist group; a printed checklist was read aloud by a nurse or nonprocedure physician with each item confirmed by operator. Checklist included 10 items that should always be performed prior to intubation. Checklist performed anytime between enrollment and induction. Could abort checklist if needed for patient safety Control group, no written checklist All other aspects the same Primary co-outcomes: lowest SpO_2 and lowest SBP between induction and 2 minutes after intubation Secondary: composite of life-threatening complications, delta in SpO_2 and SBP from induction, no. of laryngoscopy attempts,	262 patients included and analyzed. Operators included 27 pum/crit fellows and 19 anesthesia residents. All 10 checklist items performed and verbalized in 81% of patients. In the 19% who did not have all 10 items completed only 3% had more than one checklist item missing No difference in primary outcomes: SpO_2 checklist group (median 92%; interquartile range [IQR] 79-98) and usual care (93%; IQR 84-100, *P*=.34). SBP no difference (112, IQR 94-133) and (108, IQR 90-132l, *P*=.61) Most common missing checklist item was difficult airway eval. Prespecified per protocol analysis showed no difference of the 106 patients with all items completed No difference in secondary outcomes No difference in any	Indirect evidence study conducted in ICUs; also study setting (tertiary academic ICUs) and trainee operators may limit generalizability to other settings Checklist did not include fluid loading, Levo admin, preoxygenation with NIV. This trial had some penetrance of checklist items into usual care Randomization occurred at patient level. Operators could be contaminated by prior checklist intubation Trial centers had performance of some checklist items in usual care group leading to contamination

			Cormack and Lehane grade, vent free days, ICU free days, and inhospital mortality	prespecified subgroups	
Lascarrou et al (2017)[30]	III for Q1	Randomized unblinded study of VL versus DL conducted in 7 ICUs in France between May 2015 and January 2016	McGrath Mac VL versus Macintosh DL Adult ICU patients requiring orotracheal intubation The primary outcome was FPS Secondary outcomes included hypoxia (<90%) or severe hypoxia (<80%)	371 patients were randomized. The most common reason for intubation was neurologic failure followed by respiratory failure Hypoxemia occurred in 14/173 (8.1%) of VL patients and 19/174 (10.9%) of DL patients (difference, 2.8%, 95% CI –3.3% to 9.0%), *P*=.37 Severe hypoxemia occurred in 6/176 (3.4%) of VL participants and 1/181 (0.5%) of DL participants (difference 2.9%, 95% CI 0.0%-5.7%) *P*=.06 FPS occurred in 126/186 (68%) of VL participants and 130/185 (70%) of DL patients (difference 2.5%, 95% CI –6.9% to 11.9%), *P*=.60	Indirect evidence study conducted in ICUs Study was unblinded without independent outcome assessment Single device used for VL (McGrath Mac), limiting generalizability Operators included primarily nonexperts Higher rate of complications associated with VL may result from difficulties in indirect glottis visualization or operator familiarity
Lewis et al (2017)[27]	III for Q1	Systematic review and meta-analysis of VL versus DL Multiple settings including operating theaters, ICU, EDs	Studies including participants ≥16 y who required tracheal intubation during general	64 RCTs with 7,044 participants were included, only 8 studies with 1,319 patients reported hypoxia	Some indirect evidence mixed with not applicable settings because most of these intubations occurred in

		One study took place in an ICU and one in an ED. The rest took place in the operating room among elective surgical patients	anesthesia Nine types of video laryngoscopes were used including Glidescope, Pentax AWS, C-MAC, McGRath series 5, X-lite, Airtraq, Truview EVO2, and CEL-100 Primary outcomes: failed intubation or change of device required (failure as defined by the study authors) and hypoxia between start of intubation and recovery from anesthesia FPS was a secondary outcome	In an analysis of 8 studies with 1,319 participants, hypoxia was not different between the groups (OR 0.39, 95% CI 0.10-1.44, I^2=70%). Data from 36 studies with 4,731 participants demonstrated that FPS was not different between groups (OR 1.27, 95% CI 0.77-2.09, I^2 =79%)	an OR among elective surgical patients; only one study occurred in the ED High heterogeneity in hypoxia outcome Potential bias due to inability to blind operators Limited data on certain high-risk populations (eg, obese patients, ICU settings)
Perera et al (2021)[24]	III for Q1	Prospective observational study in Australia and New Zealand. 43 EDs. 17 classified as major referral (39.5%), 13 urban district (30.2%), 13 regional or rural (30.2%). 14 (32%) major trauma centers Inclusion criteria: all patients intubated in participating EDs Exclusion: intubated during cardiac arrest, received apneic BVM or NIV between induction and laryngoscopy though rescue ventilation was not an exclusion	Data reported by the intubating physician close to the time of intubation using a paper form Predefined definitions ApOx defined as provision of oxygen up to 15 LPM versus NC during apneic period between induction and MV. Humidified high-flow devices not generally available. Standard care defined as absence of NC Primary outcome:	2,831 eligible patients were analyzed. 1,669 (58.9%) had ApOx. 850 (30%) did not. Primarily performed by emergency medicine. ApOx had 10.4% patients desaturated compared to standard care 13.7% (*P*=.01) Logistic regression those receiving Apox had sig reduced likelihood of desaturation (OR 0.071, 95% CI 0.53-0.95)	Retrospective analysis of a prospectively collected database Nonrandomized. Data gathering provided by intubating MD after the fact. High risk of recall bias No standardized method of providing ApOx No standardized duration of PreOx; however model

		criterion	desaturation <93%	compared to standard	adjusted for BVM+PEEP, BVM, LMA, and NIV using NRBM as the reference standard Case deletion for missing data in lieu of imputation
Prekker et al (2023)[28]	III for Q1	Open randomized trial of VL versus DL conducted in 7 EDs and 10 ICUs	Included critically ill adults. Allocation was concealed. The study's primary outcome was FPS Secondary outcomes included severe hypoxemia (<80%) measured between induction and 2 minutes after intubation A trained observer collected outcome data	1,420 patients were enrolled and 1,417 were analyzed. 70% of patients underwent intubation in an ED. 45% of the patients had altered mental status and 30% had acute respiratory failure. 91.5% of intubations were performed by trainees. Severe hypoxemia occurred in 64/658 (9.7%) of VL patients and 69/659 (10.5%) of DL patients (difference 0.7%, 95% CI –2.7% to 4.2%). FPS occurred in 600/705 (85%) of VL participants and 504/712 (71%) of DL participants (difference 14%, 95% CI 10-19, *P*<.001)	Brand of video laryngoscope was not specified Pragmatic, unblinded study, patients requiring immediate intubation or belief that one technique over the other was preferred excluded patients; blade types used for DL were not specified; powered to detect difference in first-pass rates, not safety outcomes; no mention of whether data analysts were blinded to outcomes and interventions Indirect evidence because subgroup analysis by setting (ED/ICU) not done for the secondary endpoint

					of hypoxemia
Semler et al (2016)[22]	III for Q1	Randomized, open-label, parallel-group, pragmatic trial Inclusion: adult patients intubated in the MICU by a critical care fellow Exclusion: awake intubation, so emergent that patient could not be randomized, or if treating clinician believed that a specific approach to intraprocedural oxygenation or a specific laryngoscopy device was mandated	Intervention: AO by a HFNC set to 15 L/min of 100% which was left in place until intubation was completed Control: usual care; preoxygenation was allowed; however, supplemental oxygen (SMO) was removed during laryngoscopy Per factorial design patients were also simultaneously randomized to either VL or DL results reported elsewhere All other treatments left to the judgment of treating clinician Primary outcome: lowest SpO_2 between induction and 2 minutes after endotracheal tube placement Secondary outcomes included hypoxemia (SpO_2<90%), severe hypoxemia (SpO_2<80%), desaturation (decrease in SpO_2<3%), and change in	150 patients were enrolled SpO_2 at time of induction was 99% (IQR 96%-100%) with AO versus 98% (IQR 94%-99%) in the usual care arm (*P*=.03) Primary outcome lowest SpO_2 AO 92% (IQR 84%-99%) versus 90% (80%-96%) *P*=.016 SpO_2<90%, ApO_2 44.7% versus usual 47.2% SpO_2<80%, ApO_2 15.8% versus usual 25.0%	Indirect evidence study performed in the ICU Higher propofol use for induction in the usual care group (13.7% versus 2.5% *P*=.02) may have confounded results Unblinded study Power calculation was done for the difference in lowest SpO_2, there is a trend toward ApO_2 preventing severe hypoxia SpO_2<80% but the study was underpowered for categoric outcomes Patients were also randomized to receive VL versus DL, there is no adjustment for patients receiving these interventions in a combined factorial analysis

			baseline saturation		
Semler et al (2017)[12]	III for Q1	Multicenter randomized control trial in 4 ICUs between July 22, 2015, and July 19, 2016	Compared the ramped position (head of the bed elevated to 25°) with the sniffing position (torso supine, neck flexed, and head extended) among 260 adults undergoing endotracheal intubation by pulmonary and critical care medicine fellows Primary outcome was lowest arterial oxygen saturation between induction and 2 minutes after intubation Secondary outcomes included hypoxemia SpO_2 <90% and severe hypoxemia SpO_2<80%	N=260; 130 randomized in each group; median lowest arterial oxygen saturation was 93% (IQR 84%-99%) with the ramped position versus 92% (IQR 79%-98%) with the sniffing position (*P*=.27) Oxygen <90%: 41.7% versus 39.4% (*P*=.70); oxygen <80%: 28.3% versus 20.5% (*P*=.14)	Indirect evidence study done in ICUs; imputation for missing saturation was done using initial saturation at induction instead of with all clinical variables as suggested with multiple imputation methods; ramped position groups had more patients with hemodynamic instability; no mention of blinding for those analyzing the data; study not powered for subgroup analyses; limited assessment of the effect of different equipment types used during the intubation
Von Hellmann et al	II for Q1	Systematic review and meta-analysis conducted across various settings (ED, ICU, OR); subgroup analyses done by each setting	Included 18 studies (12 RCTs, 6 observational) with 9,151 participants. Intervention: bougie use during intubation. Outcome measures: first-attempt intubation success, complications, intubation time, hypoxemia, airway trauma. Statistical methods: random-effects models, GRADE	Bougie use was associated with higher first-attempt success (RR 1.11, 95% CI 1.06-1.17). Subgroup analysis for difficult airways (Cormack-Lehane 3 or 4) showed RR 1.60, 95% CI 1.40-1.84. No significant difference in hypoxemia or esophageal intubations	Indirect evidence with studies done in ICUs and ORs but sensitivity and subgroup analyses done by setting by combining ED and ICU data separate from OR data; high heterogeneity (I^2=83%). Risk of bias due to lack of standardization in

			evaluation	Meta-analysis of 6 studies[4,17-19,22,29] including 3,160 patients, the use of a bougie was not associated with an increased incidence of hypoxemia, but the CI was wide (RR 0.93, 95% CI 0.66-1.31, I^2=59%)	intubator training; inconsistent reporting of procedural complications; evidence quality graded low. Recommendations favor bougie-first approach, especially in emergency settings; unclear definition for hypoxia <90% and <80% were selected for included studies
Vourc'h et al (2015)[19]	III for Q1	Multicenter, randomized, open-label controlled trial conducted in 6 French ICUs	Included 124 hypoxemic adults requiring intubation with PaO_2/FiO_2<300 mmHg and respiratory rate ≥30/min. Patients were randomized to HFNC or high FiO2 facial mask (HFFM) for preoxygenation. Primary outcome: lowest oxygen saturation during intubation. Secondary outcomes: intubation-related adverse events, MV duration, and mortality	A total of 124 patients were randomized. In the ITT analysis, including 119 patients (HFNC, n=62; HFFM, n=57), the median (IQR) lowest saturation was 91.5% (80-96) for HFNC and 89.5% (81-95) for the HFFM group (*P*=.44). Severe desaturation (SpO_2=80%) was the main severe complication, with 16 (25.8%) patients in HFNC and 13 (22.3%) in HFFM (*P*=.70)	Indirect evidence study conducted in ICUs; limited power due to a small sample size; findings limited to the studied population with severe hypoxemia. HFNC was no better than HFFM in preventing desaturation but was safe and feasible
Q2					
April et al (2020)[38]	III for Q2	Secondary analysis of the data from the multicenter, prospective observational study using the NEAR data from 25 EDs in 2016-	Included normotensive (SBP between 100 and 140 mmHg) ED patients (>14 y) induced with	738 encounters with ketamine, and 6,068 encounters with etomidate Etomidate was more	Observational design limits causality; possible confounding due to ketamine being

		2018	ketamine or etomidate Primary outcome measure was the incidence of peri-intubation hypotension (SBP<100 mmHg) Secondary outcomes were the incidence of peri-intubation hypotension requiring intervention and mortality	commonly used for "medical" indications, (75% versus 67%), and ketamine more commonly for trauma (33% versus 25%) Peri-intubation hypotension incidence was 18.3% among patients receiving ketamine and 12.4% among patients receiving etomidate (effect size 5.9%, 95% CI 2.9%-8.8%) Logistic regression analysis also showed a higher risk of postintubation hypotension among patients receiving ketamine (adjusted odds ratio [aOR] 1.4; 95% CI 1.2-1.7), and a higher risk of treatment for hypotension. (aOR 1.8; 95% CI 1.4-2.0) There was no dose-related effect for either agent (ketamine <1 versus >1 mg/kg or etomidate 0.3 versus >0.3 mg/kg)	used in sicker patients with sepsis or trauma. Propensity score matching to adjust for selection of induction agents was not undertaken; methods do not account for preintubation hypotension
Driver et al (2023)[41]	III for Q2	Secondary analysis of the prospective observational study using the NEAR data from 25 EDs (2016-2018)	Included ED patients (>14 y) induced with ketamine or etomidate Primary outcome measure was the incidence of peri-	14,024 intubations were included, 86.8% used etomidate and 13.2% used ketamine The multivariable models	Observational design limits causality. Actual body weight used for dosing may not reflect clinical practice using lean body weight.

			intubation hypotension (SBP<100 mmHg) in the 15 minutes following intubation Secondary outcomes were the incidence of postintubation hypotension treated with IVF or vasopressors	demonstrated that neither etomidate dose per 0.1 mg/kg (aOR 0.95, 95% CI 0.90-1.01) ketamine dose per 1 mg/kg (aOR 0.97, 95% CI 0.81-1.17) were associated with postintubation hypotension Similarly, neither etomidate dose (aOR 0.94, 95% CI 0.89-1.00) nor ketamine dose (aOR 0.91, 95% CI 0.75-1.10) was significantly associated with postintubation hypotension treated with fluids or vasopressors	Hypotension recorded as binary outcome without pre/post blood pressure trends; sensitivity analyses attempted to adjust for missing data and confounders related to selection of induction agents but without use of propensity scoring
Ferguson et al (2022)[34]	II for Q2	Multicenter ED-based RCT of fentanyl versus placebo in addition to ketamine and rocuronium	Primary outcome was postintubation SBP outside the range of 100-150 mmHg (or if they were hypotensive at induction, a drop in SBP>10% within the first 10 minutes)	302 patients were randomized; 290 analyzed, but 13/290 did not have follow-up data; 277 in final analysis 29% of patients in the fentanyl group had at least one SBP measurement <100 mmHg compared with 16% of the placebo group (difference 13%; 95% CI 3%-23%)	Patients were not recruited overnight due to staffing limitations; missing data addressed with sensitivity analysis assuming all have extreme outcomes; CONSORT diagram did not include loss to follow-up; study was powered for the primary outcome of SBP out of range; hypotension outcome did not adjust for multiple

					comparisons for CI reporting
Ishimaru et al (2019)[40]	III for Q2	Secondary analysis of prospective multicenter observational study (JEAN-2 registry) across 15 EDs in Japan (2012-2017)	Included hemodynamically unstable ED patients, as defined by a preintubation SI of ≥0.9, who were induced with ketamine, midazolam, or propofol The primary outcome measure was postintubation hypotension (SBP<90 mmHg) during 30 minutes postintubation or ≥20% decrease in SBP between pre- and postintubation period	977 patients were included Overall, the incidence of postintubation hypotension was 23% Ketamine was more commonly used for medical shock patients, (53% versus 22%), and less likely to be chosen for respiratory failure (24% versus 37%) Postintubation hypotension: 15% (ketamine) versus 27% (reference); aOR 0.43 (95% CI 0.29-0.65), *P*<.001. Propensity-matched analysis confirmed lower risk with ketamine (OR 0.47, 95% CI 0.31-0.71)	Observational design limits causality. Lack of post-ED outcome data. Potential unmeasured confounders (eg, fluid/vasopressor use). Findings may not generalize to non-Japanese ED settings. No blinded abstraction

Janz et al (2019)[43]	III for Q2	Unblinded randomized trial in 8 ICUs and 1 ED	Patients received either an intravenous bolus of 500 mL of crystalloid solution initiated prior to induction, versus no bolus Patients were excluded if treating clinicians felt administration of a fluid bolus was required or contraindicated The primary outcome was cardiovascular collapse (SBP<65 mmHg), new or increased vasopressor use between induction and 2 minutes postintubation, or cardiac arrest or death with an hour of intubation	337 patients were included The primary endpoint did not differ between the fluid bolus group and the no fluid bolus group (20% versus 18%, absolute difference of 1.3%; 95% CI –7.1% to 9.7%, *P*=.76). There was no difference between the fluid bolus group and the no fluid bolus group in the subgroups of patients with sepsis shock (RR 0.91; 95% CI 0.48-1.72) or on vasopressors (RR 0.91; 95% CI 0.48-1.71)	Mainly ICU patients Outcome measure of cardiovascular collapse was more stringent than peri-intubation hypotension used in other studies Patients were excluded in cases where the treating physician judged them to need a fluid bolus Unclear how much fluid patients received preceding enrollment in the study
Knack et al (2023)[36]	III for Q2	Single-center, randomized, parallel-group trial of ED intubations	Patients were induced with ketamine (2 mg/kg) or etomidate (0.3 mg/kg) Primary outcome measure was maximum SOFA score during the first 3 days of hospitalization Exploratory outcome measures included postintubation hypotension (SBP<90 mmHg) at any time after intubation while still in the ED, or, separately, within 6 hours	143 patients were included The most common indication for intubation was medical (53%), and the average preintubation SBP was 140 mmHg The incidence of hypotension in the ED was 28% in the ketamine group and 26% in etomidate group (difference 2%, 95%	Small sample size may limit generalizability. Excluded women of childbearing age in the latter part of the trial. Emergency physician unblinding may affect outcomes. Conducted 7 y prior to publication; baseline imbalances in difficult airway characteristics, sepsis criteria, sedatives administered prior to intubation

			of intubation	CI –13% to 17%)	
Russell et al (2022)[44]	III for Q2	Multicenter, parallel-group, unblinded, pragmatic, randomized trial in 11 ICUs	Included adults intubated with planned use of PPV between induction and laryngoscopy Patients excluded if fluid bolus was either needed or contraindicated Intervention group received 500 mL of isotonic crystalloid, with as much being infused prior to intubation without delaying the procedure, the remainder was infused after Primary outcome was cardiovascular collapse (new or increased vasopressors or SBP<65 mmHg between induction and 2 minutes after intubation, cardiac arrest or death within 1 hour after intubation) Secondary outcomes included O_2 saturation <90% and <80%	1,065 patients randomized and included; 538 received fluid bolus, 527 controls 113 patients (21%) in the fluid bolus group versus 96 (18.2%) controls had cardiovascular collapse (difference 2.8%, 95% CI –2.2% to 7.7%) 33.5% in fluid bolus group O_2 saturation <90% compared with 29.7% controls (difference 3.8, 95% CI –2.0 to 9.6) 14.9% in fluid bolus group O_2 saturation <80% compared with 13.7% controls (difference 1.2, 95% CI –3.3 to 5.6)	Indirect evidence ICU patients 15% patients excluded due to urgency of intubation Patients were excluded in cases where the treating physician judged them to need a fluid bolus Unclear how much fluid patients received preceding enrollment in the study Pragmatic unblinded RCT but analysts were blinded to treatment Models did not adjust for different preoxygenation strategies but they are listed in the supplements
Smischney et al (2019)[39]	III for Q2	Single-center, stratified, RCT at a tertiary academic medical center ICU (July 2014 to October 2017)	Patients were induced with a 50 μg of intravenous bolus of fentanyl plus	160 patients were included There was no statistically	Single-center limits generalizability. Nonblinded

			either equal parts ketamine/propofol admixture (KPA) (1 mg/kg) or reduced dose etomidate (0.15 mg/kg) Primary outcome measure was the change in mean arterial pressure (MAP) from baseline, 5 minutes after drug administration. Secondary outcomes included the change in MAP at 10 and 15 minutes from baseline	significant difference in the 5-minute MAP as compared with the baseline in either the KPA (77.6 ±15.4 mmHg versus 80.9 ±13.3 mmHg at baseline) or the etomidate group (81.7 ±17.2 mmHg versus 82.8 ±17.9 mmHg at baseline) (treatment difference, −2.1 mmHg; 95% CI, −6.9 to +2.7 mmHg; *P*=.385)	interventions and cointerventions may introduce bias. Small sample size limits statistical power for subgroup analyses. Excluded baseline cortisol data, impacting adrenal function assessments
Takahashi et al (2018)[42]	III for Q2	Secondary analysis of multicenter prospective study (JEAN-2) in 14 Japanese EDs (2012-2016)	Included ED patients (with a preintubation SBP >90 mmHg) undergoing emergent intubation Patients were divided into fentanyl and non-fentanyl groups The primary outcome measure was postintubation hypotension (any recorded SBP of ≤90 mmHg during the 30-minute period following intubation in the ED)	1,263 patients were included Fentanyl was used as a pretreatment medication of RSI in 466 patients (37%) Fentanyl was more likely to be used for patient intubated for shock (22% versus 12%), and less likely to be used for respiratory failure (30% versus 52%) Overall, 125 patients (10%) experienced postintubation hypotension Patients who received fentanyl had a higher risk of postintubation hypotension compared with	Observational design limits causality. Possible unmeasured confounders (eg, fluid resuscitation, vasopressor use). No post-ED outcomes (eg, mortality). Self-reported data may underestimate hypotension rates. Limited generalizability outside Japanese EDs

				those who did not receive fentanyl (17% versus 6%) (OR 1.73; 95% CI 1.01-2.97; *P*=.048) Multivariable model also found a higher risk of postintubation hypotension with fentanyl pretreatment (aOR, 1.87; 95% CI 1.05-3.34; *P*=.03) Propensity score-matched analysis showed OR 3.17 (95% CI 1.96-5.14, *P*<.01)	
Zed et al (2006)[37]	III for Q2	Prospective observational study conducted over 42 months at a tertiary care teaching hospital ED in Vancouver, Canada	Included 522 adult ED patients receiving etomidate (0.3 mg/kg) for RSI. Primary outcomes: intubating conditions (sedation/paralysis, technical difficulty) and hemodynamic effects (SBP, DBP, HR preintubation and postintubation, with subgroup analysis for SBP <100 mmHg)	491 patients were included The most common indication for intubation was trauma (37%) 26% were pretreated with fentanyl Overall, there was an elevation in SBP from a mean of 133 to 138 mmHg (*P*<.0001) and DBP from 70 to 72 mmHg (*P*=.0002) immediately postintubation with etomidate In the subgroup who were hypotensive preintubation, SBP improved from a mean of 82 to 94 mmHg at 5	Noncomparative design; adrenal suppression not evaluated. Subjective Likert scales used for intubating conditions may introduce variability. Results may not generalize beyond tertiary care ED settings

				minutes (P<.0001)	

AO, apneic oxygenation; *ASA*, American Society of Anesthesiologists; *BVM*, bag-value mask; *CI*, confidence interval; *CONSORT*, Consolidated Standards of Reporting Trials; *COT*, conventional oxygen therapy; *DBP*, diastolic blood pressure; *ED*, emergency department; *EMS*, emergency medical service; *FPS*, first pass success; *GRADE*, Grading of Recommendations Assessment, Development and Evaluation; *HFNC*, high-flow nasal cannula; *HR*, heart rate; *ITT*, intention-to-treat; *IVF*, intravenous fluids; *LMA*, laryngeal mask airway; *LOS*, length of stay; *MICU*, medical intensive care unit; *MV*, mechanical ventilation; *NC*, nasal cannula; *NEAR*, National Emergency Airway Registry; *NIV*, noninvasive ventilation; *NMB*, neuromuscular blockade; *NP*, nasal passage; *NRBM*, nonrebreather bag-value mask; *PEEP*, positive end-expiratory pressure; *PPV*, positive pressure ventilation; *RR*, respiratory rate; *SBP*, systolic blood pressure; *SI*, shock index; *SMO*, supplemental oxygen; *SOFA*, sequential organ failure; *VAP*, ventilator-associated pneumonia.